IN THE UNITED STATES PATENT AND TRADEMARK OFFICE BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

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Applicants : Hiroyuki ASADA et al.

Serial No. : 10/524,996

Filed : February 18, 2005

For : STABLE OPHTHALMIC SOLUTION COMPRISING LATANOPROST AS...

Art Unit : 1612

Examiner : Walter E. WEBB

Docket No. : 05105/HG

Confirm. No.: 3212

Customer No.: 01933

REPLY BRIEF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313

MAIL STOP APPEAL BRIEFS - PATENTS

S I R :

This is responsive to the EXAMINER'S ANSWER mailed March 3, 2010.

This Reply Brief is being timely filed within two months of the EXAMINER'S ANSWER, by the due date of May 3, 2010.

REMARKS

1. On page 4, lines 13 to 18 of the EXAMINER'S ANSWER, the Examiner alleged that it would have been obvious to a person having ordinary skill in the art to add a known stabilizing agent, such as ε-aminocaproic acid at 0.01 - 2.0% to the composition of Schneider et al., motivated by the teachings of Kimura et al. that ε-aminocaproic acid would suppress formation of agglomerates, prevent lowering of pH and provide a suspension superior in redispersibility and stability.

It is respectfully submitted, however, that the above allegation in the EXAMINER'S ANSWER is not correct, because the composition to be stabilized is completely different between Schneider et al. and Kimura et al. The Schneider et al. composition is an aqueous solution of a prostaglandin (see column 7, line 47; column 8, line 15; and column 9, line 42 of Schneider et al.), whereas the Kimura et al. composition is a suspension (see the Abstract of Kimura et al., and see column 1, line 50; column 2, lines 17, 28 and 51; column 3, lines 19 and 34; and column 4, lines 12, 21 and 36 of Kimura et al.). It was admitted on page 4, lines 11 to 12 of the EXAMINER'S ANSWER, that Kimura et al. do not teach the use of latanoprost. Rather, the active ingredient in Kimura et al. is difluprednate.

Therefore, it is respectfully submitted that a person having ordinary skill in the art would not consider that the stabilizing technology for a suspension of difluprednate is applicable to the stabilizing technology for an aqueous solution of a prostaglandin.

2. With respect to the last full paragraph on page 5 of the EXAMINER'S ANSWER, it is respectfully submitted that the Examiner's interpretation of the teachings of Kimura et al. is incorrect.

Kimura et al. do not teach that ε-aminocaproic acid can increase the chemical stability of active ingredients. The reason is as follows:

(1) The problem that Kimura et al. sought to address involved the possibility that their suspension of difluprednate may form secondary particles, due to partial agglomeration caused by mutual adhesion of suspended particles, or a hard deposit layer (caking) on the bottom surface of a container; or may have a lowered pH when left standing for a long time (see column 1, lines 53 to 58 of Kimura et al.). Kimura et al. do not mention the chemical stability of difluprednate (active ingredient). The aim of Kimura et al. is to block the pH lowering of a suspension (see column 1, lines 61 to 67 of Kimura et al.).

(2) Therefore, Kimura et al. did not check the stability of difluprednate. Kimura et al. merely observed the pH of their

suspensions in their working examples.

(3) In Kimura et al., ε-aminocaproic acid was always used with a suspending agent, such as HPMC and polysorbate 80 as shown in Table 1 in column 6 of Kimura et al. Concerning ε-aminocaproic acid, no single effect was examined in Kimura et al.

The following was stated in column 7, lines 7 to 13 of Kimura et al.:

> "The above results demonstrate that the combination of HPMC as a suspending agent and sodium acetate or ε-aminocaproic acid as a buffer makes the suspension stable and such stability can be maintained even if benzalkonium chloride and chlorhexidine gluconate are added as preservatives and sodium chloride is added as an isotonizing agent. The addition of a surfactant did not affect said stability."

Applicants respectfully submit that the gist of the Kimura et al. invention is set forth in the preceding paragraph

Applicants respectfully submit that based on the teachings of Kimura et al., the efficacy of pure ε-aminocaproic acid is not known. Furthermore, based on the teachings of Kimura et al., it is respectfully submitted that the efficacy of ε-aminocaproic acid on the chemical stability of diflupredrnate (active ingredient) would not be known. Therefore, applicants respectfully submit that it would not be obvious to add ε-aminocaproic acid for increasing the stability of a latanoprost aqueous solution.

3. The following was stated on page 5, lines 12 to 15 of the EXAMINER'S ANSWER:

> "Adding ε-aminocaproic acid would have been obvious, since it is known in the prior art as useful for suppressing formation of agglomerates, preventing lowering of pH and providing a suspension in redispersibility and stability."

It is respectfully submitted that the above contention is incorrect, since it is necessary to understand the Kimura et al. invention and to understand the meaning of "stability." Kimura et al. do not teach that ε-aminocaproic acid will increase the chemical stability of an active ingredient.

4. The following is stated on page 5, lines 15 to 17 of the EXAMINER'S ANSWER:

> "Kimura et al. teaches the use of a different active agent, but the artisan would reasonably expect ε-aminocaproic acid to provide the same stability in the ophthalmic suspension of Schneider et al."

It is respectfully submitted that the Examiner misunderstood the teachings of Schneider et al.

As discussed hereinabove, whereas Schneider et al. concern an aqueous solution (not a suspension), Kimura et al. relate to a suspension. Therefore, it is respectfully submitted that a person of ordinary skill in the art would not expect ε-aminocaproic acid to provide the same stability as in Kimura et al.

5. The following was stated on page 5, lines 18 to 20 of the EXAMINER'S ANSWER:

> "...and the fact that ε-aminocaproic acid is listed among other ophthalmic components taught in Schneider such as castor oils and sodium acetate (see Schneider, column 8, lines 1 to 15)."

The above allegation is incorrect. As admitted on page 4, lines 1 to 2 of the EXAMINER'S ANSWER, there is no disclosure of ε-aminocaproic acid in Schneider et al. Thus, ε-aminocaproic acid is not listed among other ophthalmic components taught in Schneider et al., such as castor oils and sodium acetate (see column 8, lines 1 to 15 in Schneider et al.).

6. The following was set forth on page 6, lines 5 to 7 of the EXAMINER'S ANSWER:

> "However, the increased stability is viewed as being expected insofar as ε-aminocaproic is recognized in the art as a stabilizing agent for ophthalmic formulations."

As discussed hereinabove, the Examiner's understanding of the teachings of Kimura et al. is incorrect. Therefore, it is respectfully submitted that an increase in stability would not be expected.

7. The following was stated on page 6, lines 15 to 17 of the EXAMINER'S ANSWER:

"It is also unclear how the storage time and temperatures relate to storage at room temperature generally."

It is respectfully submitted that the document submitted with applicants' AMENDMENT FILED CONCOMITANTLY WITH RCE filed on April 17, 2008, namely, "Stability of Drugs and Dosage Forms," explains the shelf-life estimation from temperature accelerated studies. Applicants have informed the undersigned that they used such temperature accelerated studies for the data set forth in the present specification.

An English-language translation of a portion of page 42 of the aforesaid "Stability of Drugs and Dosage Forms" is set forth on page 8 of applicants' AMENDMENT FILED CONCOMITANTLY WITH RCE filed April 17, 2008.

8. In the paragraph bridging pages 6 to 7 of the EXAMINER'S ANSWER, the position was taken that the "instant claims are not commensurate in scope" with the data set forth in the specification.

Applicants respectfully disagree with the above allegation. The results shown in Table 1 on page 10 of the specification, and in Figs. 1 and 2, are commensurate with applicants' claimed pH range of 5.0 to 6.25.

9. The following was set forth on page 7, lines 4 to 6 of the EXAMINER'S ANSWER:

> "The results are also inconsistent in regard to pH, since formulations 1-8 are shown to have a pH of 7, while the instant claims 12, 14 and 16 are limited to a pH of 5.0 to 6.25."

For the following reasons, applicants respectfully disagree with the above contention.

Applicants' claim 12 recites the following:

> "pH of the solution ... 5.0 to 6.25 and ... ε-aminocaproic acid."

Applicants' claim 12 is a combination of two features, namely, (i) a pH of 5.0 to 6.25 and (ii) the addition of ε-aminocaproic acid.

Applicants' claim 12 is fully supported in the specification and fully consistent with the disclosure in the specification. In this regard, see page 4, lines 2 to 4 of the specification, which state as follows:

> "Of course, pH can be adjusted to 5.0 to 6.25 and ε-aminocaproic acid can be added as the additive at the same time, and thereby their synergistic effect can be obtained."

The data in the present specification demonstrates that a pH of 5.0 to 6.25 can stabilize a latanoprost aqueous ophthalmic solution, and that ε-aminocaproic acid can stabilize a latanoprost aqueous ophthalmic solution at a pH of 7, also. It is therefore respectfully submitted that a person of ordinary skill in the art would understand from applicants' data that a latanoprost aqueous ophthalmic solution can be stabilized by the addition of ε-aminocaproic acid to a latanoprost aqueous ophthalmic solution at a pH of 5.0 to 6.25.

10. The following was stated on page 7, lines 2 to 4 of the EXAMINER'S ANSWER:

> "Appellant's claims are drawn to storage at room temperature, which is commonly between 20°C to 25°C, and do not recite time of storage."

It is not necessary that applicants' claims recite a time for storage, since a time for storage involves results of the presently claimed invention. It is noted that advantages inherent in a claim which renders the claim patentable over the prior art need not be recited in the claims. In re Estes, (CCPA 1970) 164

USPQ 519 and In re Merchant, (CCPA 1978), 197 USPQ 785, 788 which states as follows:

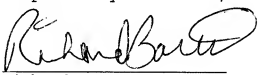
> "We are aware of no law requiring unexpected results relied upon for patentability be recited in the claims."

CONCLUSION

In view of the foregoing and the Appeal Brief filed September 30, 2009, it is respectfully submitted that each of claims 6, 8, 10, 12, 14 and 16 all clearly patentably distinguish over Schneider et al. and Kimura et al., taken singly or in any combination under 35 USC 103.

It is therefore respectfully requested that this Board reverse the rejection of appealed claims 6, 8, 10, 12, 14 and 16.

Respectfully submitted,



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